Susceptibility-Weighted Imaging Identifies Iron-Oxide-Labeled Human Neural Stem Cells: Automated Computational Detection.

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Public Summary:
Neonatal brain injury due to hypoxia can lead to devastating neurological outcomes such as cerebral palsy, epilepsy and mental retardation. Human neural stem cell therapy provides new hop for its treatment.These multipotent cells can aid in HII recovery by activating multiple reparative mechanisms including secretion of neurotrophic factors that enhance brain repair and plasticity. For clinical use of implanted hNSCs, methods are required to identify, quantify, track, and visualize migration and replication in an automated and reproducible fashion. Susceptibility weighted imaging can provide an advanced MRI method that will allow visualization of hNSCs within affected regions of the injured neonatal brain.

Scientific Abstract:
Neonatal hypoxic-ischemic brain injury (HII) can lead to devastating neurological outcomes such as cerebral palsy, epilepsy, and mental retardation. Human neural stem cell (hNSC) therapy provides new hope for the treatment of neonatal HII. These multipotent cells can aid in HII recovery by activating multiple reparative mechanisms including secretion of neurotrophic factors that enhance brain repair and plasticity. For clinical use of implanted hNSCs, methods are required to identify, quantify, track, and visualize migration and replication in an automated and reproducible fashion. In the current study, we used a model of unilateral HII in 10-day-old rat pups that were implanted with 250,000 Feridex-labeled hNSCs into the contralateral ventricle 3 days after HII. In addition to standard noninvasively acquired serial magnetic resonance imaging (MRI) sequences (11.7 and 4.7 T) that included diffusion-weighted imaging and T2-weighted imaging, we also acquired susceptibility-weighted imaging (SWI) 1-90 days after hNSC implantation. SWI is an advanced MRI method that enhances the visualization of iron-oxide-labeled hNSCs within affected regions of the injured neonatal brain. hNSC contrast was further enhanced by creating minimal intensity projections from the raw SWI magnitude images combined with phase information. Automated computational analysis using hierarchical region splitting (HRS) was applied for semiautomatic detection of hNSCs from SWI images. We found hNSCs in the ipsilateral HII lesion within the striatum and cortex adjacent to the lesion that corresponded to histological staining for iron. Quantitative phase values (radians) obtained from SWI revealed temporally evolving increased phase which reflects a decreased iron oxide content that is possibly related to cell division and the replicative capacity of the implanted hNSCs. SWI images also revealed hNSC migration from the contralateral injection site towards the ipsilateral HII lesion. Our results demonstrate that MRI-based SWI can monitor iron-labeled hNSCs in a clinically relevant manner and that automated computational methods such as HRS can rapidly identify iron-oxide-labeled hNSCs.